and binding studies using real time kinetics and surface plasmon resonance of these proteins have shown several features that are important for signaling roles of IGF and SPX-40. The detailed study of various structural characterstics of LF and LP have revealed their new functions and have helped in the understanding of the mechanism of their action. IGF is a signaling component secreted during proliferative phase and its structure showed many novel features pertaining to structure and function relationship. We have also studied the structures of C-terminal halves of LF and their various complexes with tight binders of C-lobe and NSAIDs. It indicates a new role of lactoferrin C-lobe as a protector of side effects of NSAIDs. The structural studies of PGRP have revealed that this protein existed in a tetrameric form with four structurally identical molecules giving rise to a potent and versatile binding site.

**1279-Pos Board B49**
**Design of Protein Sequences which Fold into Secondary Structures using an Explicit Solvent Model**
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The folding of proteins into helices and beta sheets has been investigated for the past five decades. To date, there has not been a thorough understanding of the physics behind this. Theoretical predictions by Zimm and Bragg give us some information but many studies have revealed contradicting results. For example short chain polyalanine, which according to Zimm and Bragg should form a random coil forms an unusually stable helix in solution and some peptides which have a low propensity for helix formation according to the theory tend to form stable helices. In the current work we seek the helix and beta sheet forming properties of individual short peptides using a simplistic model with explicit solvent through Monte Carlo simulations. The protein back bone and side chains are represented as either hard spheres (hydrophobic) or Jagla particles (hydrophilic) in a Jagla solvent. The helix and beta sheet forming tendencies are studied while varying the chain length, backbone sequence, size of the side group and the strength of the interactions.

**1280-Pos Board B50**
**Is the Amino Acid Dipeptide a Suitable Model for Investigating Structural Preferences in the Unfolded State?**
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In view of many observations of local order within unfolded peptides and proteins, intrinsic conformational propensities of individual amino acid residues have been warranted for an understanding of how the conformational distributions in unfolded proteins affect protein folding. Various and sundry experimental and computational techniques have produced conflicting conformational sampling distributions even when similar unfolded model systems were employed. One of the most utilized model systems have been the amino acid dipeptides because the classical definition of the unfolded state was supported by the Ramachandran plot of the alanine dipeptide, which exhibited a nearly homogeneous sampling of sterically allowed conformations. Many studies on amino acid dipeptides have indicated that conformational preferences vary between different amino acids. In order to quantify these differences, we measured the amide I' band profiles of dipeptides in water using infrared absorption, vibrational circular dichroism, and Raman spectroscopy. A conformational distribution model was utilized in order to reproduce all experimental data, which was further constrained by 3J(NHN$\alpha$) and 1J(C'C$\alpha$) coupling constants. For alanine, our results suggest that it samples much less PPII-like conformations in a dipeptide than in GAG. Our experimental results were confirmed by results from Molecular Dynamics simulations. A first analysis of data obtained for other dipeptides also suggest reduced PPII fractions. We tentatively assign this to different hydration shells of blocked and unblocked peptides.

**1281-Pos Board B51**
**Conservation of Complex Knotting and Slipknotting Patterns in Proteins**
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The last decade has shown that there are an increasing numbers of known proteins that contain linear open knots or slipknots in their native folded structure. In general, knots in proteins are orders of magnitude less frequent than would be expected for random polymers with similar length, compactness, and flexibility. Explaining why they are so rare is an intriguing question. While analyzing all available protein structures for the presence of knots and slipknots we detected a surprising conservation of complex knotting patterns within and between several protein families despite their large sequence divergence. Since protein folding pathways leading to knotted native protein structures are slower and less efficient than those leading to unknotted proteins with similar size and sequence, the strict conservation of the knotting pattern in some families of proteins indicates an important physiological role of knots and slipknots in these proteins. Although little is known about the functional role of knots, recent studies have demonstrated a protein-stabilizing ability of knots and slipknots. In the slipknots studied here, some of the conserved knotting patterns occur in transmembrane domains of proteins, suggesting that slipknots may stabilize these domains against forces acting during their translocation through protein lined membrane pores.

## Protein Aggregates I

**1282-Pos Board B52**
**Is the Prevention for Alzheimer's Already in Your Medicine Cabinet?**
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Alzheimer's disease (AD) is characterized by the excessive production of amyloid protein and deposition in senile plaques, which are mainly composed of 1-40 amyloid $\beta$-proteins (A$\beta$40). Various natural mutations of Alzheimer's $\beta$-amyloid have been shown to promote an early onset of AD. Recent studies have shown that the Wild Type mutation (A$\beta$22-35) enhances neurotoxicity of 40-residue A$\beta$(1-40). Our interest is to use this shorter (14 residue) fragment of the A$\beta$. Silymarin, a mixture of flavonolignans extracted from the seeds, fruits, and leaves of Milk Thistle, has long been used for the treatment of hepatic disorders, most commonly for liver diseases. Many studies have investigated the inhibitory effects of various flavonoids on A$\beta$ aggregation and neurotoxicity. As a result, silymarin, being a mixture of flavonolignane diastereomers and having already been proven safe for human consumption, might be capable of having a preventative effect against the A$\beta$-dependent phenotypes of AD.
To identify silymarin as a potential therapeutic agent for the treatment of Alzheimer's disease, various Attenuated Total Reflection Infrared Spectroscopy, ATR-IR,and Ultraviolet Visible Spectroscopy, UV-Vis, assays will be developed to identify and rank whether or not the mixture of flavonolignane diastereomers could inhibit aggregation of A$\beta$. To carry out this test, A$\beta$ will be incubated with the test compound silymarin at a controlled temperature for a set amount of hours followed by ultrafiltration in order to separate the monomeric A$\beta$ from its aggregates. Aliquots of the ultrafiltrate will be analyzed for monomeric A$\beta$.

**1283-Pos Board B53**
**Myosin Storage Myopathy Mutations Cause Age Dependent Muscle Degeneration and Cardiac Dysfunction in a Drosophila Model**
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Myosin storage myopathy (MSM) is a rare congenital disorder caused by missense mutations in the beta cardiac MHC rod and characterized by subsarcolemmal accumulation of beta cardiac MHC that has a hyaline appearance. These mutations map near to or within the assembly competence domain known to be crucial to filament assembly. We hypothesize that mutations interrupt assembly of coiled-coil rod dimers or thick filaments causing aggregation. We have made a *Drosophila* model for MSM whichcan serve as a powerful model for mechanistic investigations. This *in vivo* model makes it possible to examine interactions between wild-type and mutant full-length myosins, as the majority of mutant alleles are dominant. We introduced the R1845W, L1793P or the E1883K mutation into a *Drosophila* myosin heavy chain transgene and expressed it in the indirect flight/jump muscles. Our studies show a severe reduction in the flight and jump ability of the transgenic flies ($p<0.0001$) in both homozygotes and heterozygotes, with an age-dependent loss of muscle function. Electron and confocal microscopy of the indirect flight muscles of transgenic lines show myofibrillar disarray with large areas of granular/ filamentous inclusions similar to hyaline bodies found in affected humans. In addition, heterozygotes of at least two mutants show restrictive cardiomyopathy phenotypes with arrhythmia that mirrors cardiomyopathy reported in human